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| EXAMINER | |
|---|---|
| NIEBAUER, RONALD T | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/574,994 | DIAMOND ET AL. | |
| | Examiner | Art Unit | |
| | RONALD T. NIEBAUER | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *23,25,45-48,51 and 54-57* is/are pending in the application.

4a) Of the above claim(s) *54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,25,45-48,51,55-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants amendments and arguments filed 4/12/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. In particular, the 112 2nd, 112 1st, 102, and double patenting rejections set forth in the previous office action are withdrawn due to the claim amendments.

Previously, Applicant's elected without traverse a peptide/mimetic/agent comprising Asp-Tyr-Glu-Tyr-Ser in the reply filed on 2/19/09.

As discussed below, the elected species was found in the prior art and the instant claims are rejected. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species. Claims 54 reads on a non-elected species.

Claim 54 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/19/09.

Claims 1-22,24,26-44,49-50,52-53 have been cancelled.

Claims 23,25,45-48,51,55-57 are under consideration.

### *Claim Rejections - 35 USC § 112*

This 112 2nd rejection is a new rejection necessitated by applicants amendments.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claim 51** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 refers to the limitation "mimetic" in claim 46. There is insufficient antecedent basis for this limitation in the claim. Claim 46 does not recite a mimetic.

Although unclear (see 112 2nd) the mimetic referred to in claim 51 is interpreted as the peptide of claim 46.

***Claim Rejections - 35 USC § 103***

Claims were previously rejected under 103 based on the references cited below. Since the claims have been amended and new claims added the rejection is updated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 23,25,45-48,51,55-57** are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaynor et al (US 6,001,964 as cited in IDS 2/19/09) and Degiorgio et al (Nature Medicine 'A subset of lupus anti-DNA antibodies cross-reacts with the NR2 glutamate receptor in systemic lupus erythematosis' 2001 v30 pages 1189-93 as cited in IDS 1/31/07).

Gaynor teach methods of treating systemic lupus erythematosis ultilizing peptides (abstract).

Gaynor does not teach in a single embodiment the administration of the elected peptide nor the administration to the brain. Gaynor does not teach in a single embodiment the determination of whether the patient has anti-NR2 antibodies.

Gaynor teach methods of treating systemic lupus erythematosis (SLE) ultilizing peptides (abstract). Gaynor teach that diagnosis of SLE is difficult without laboratory tests and teach that antibodies directed to double-stranded DNA (dsDNA) are diagnostic of SLE (column 1 lines 20-25). Gaynor teach a method for treating systemic lupus erythematosis in a subject in need of such treatment comprising administering to the subject at least one peptide which binds to an anti-double stranded DNA antibody (column 2 lines 20-25) and specifically teach the method for humans (column 6 lines 64-66). Gaynor teach various peptides that carry out such function (column 3 lines 60 - column 4 lines 40). Gaynor specifically teach a peptide of sequence Asp-Trp-Glu-Tyr-Ser (claims 9,44, column 9 line 11). Gaynor teach that the peptides neutralize

antibodies which are important in the pathogenesis of SLE (column 7 lines 4-10). Gaynor teach that the compositions can be administered using procedures known in the art including a variety of administration modes (column 7 lines 12-20). Gaynor further teach that the peptides can be delivered to the site of action by injection (column 7 lines 30-40).

Degiorgio teach that in systemic lupus erythematosis (SLE) that antibodies against double-stranded DNA are a major contributor to disease (abstract) and correlate with disease (page 1189 first column). Degiorgio teach that pentatpeptides which have previously been identified mimic the double stranded DNA (abstract). Degiorgio teach that the consensus sequence is present in NMDA receptors NR2a and NR2b (page 1189 fitst column -second column connecting paragraph). Degiorgio teach that antibodies from lupus patients were isolated and were found to bind dsDNA (page 1190 2nd column, Figure 3). Degiorgio conclude that lupus sera contains antibodies to the NMDA receptors NR2a and NR2b (page 1190 2$^{nd}$ column). Degiorgio teach that cerebrospinal fluid of patients with lupus was also tested (page 1190 2$^{nd}$ column last paragraph). Degiorgio teach that cerebrospinal fluid of a patient with lupus contains anti-DNA antibodies (abatract). Degiorgio noted that the antibodies may be produced in the brain or may cross the blood brain barrier (page 1191 paragraph connecting column 1 and 2). Degiorgio teach that up to 80% of lupus patients experience symptoms including cognitive decline (page 1189 first paragraph).

Since Gaynor teach a method for treating systemic lupus erythematosis in a subject in need of such treatment one would be motivated to treat such patients. Thus one would be motivated to patients with lupus. It is noted that such patients (patients with lupus) are at risk for lupus-induced cognitive dysfunction since as the name implies it is induced by lupus. Further,

since Degiorgio teach that up to 80% of lupus patients experience symptoms including congnitive decline (page 1189 first paragraph) one would be motivated to treat those with lupus who have cognitive decline. Thus the references motivate treating the patients recited in claims 56-57 of the instant claims. Since Gaynor teach a method for treating systemic lupus erythematosis in a subject in need of such treatment comprising administering to the subject at least one peptide which binds to an anti-double stranded DNA antibody (column 2 lines 20-25) and specifically teach the method for humans (column 6 lines 64-66) one would be motivated to administer peptides to humans with systemic lupus erythematosis as recited in claim 23. Since Gaynor specifically teach a peptide of sequence Asp-Trp-Glu-Tyr-Ser (claims 9,44, column 9 line 11) and use that specific peptide in Figure 3 one would be motivated to administer the peptide Asp-Trp-Glu-Tyr-Ser thus meeting the limitations recited in claim 55. It is noted that claim 25 refers to the location of a neuron. However, such claim does not require additional steps to be performed. Since Gaynor teach peptides which bind to an anti-double stranded DNA antibody (column 2 lines 20-25) including the elected peptide such peptides would have the function as recited in claim 25.

Gaynor teach methods of treating lupus specifically systemic lupus erythematosis (abstract, column 2 lines 20-25). Since Gaynor teach that diagnosis of SLE is difficult without laboratory tests and teach that antibodies directed to double-stranded DNA (dsDNA) are diagnostic of SLE (column 1 lines 20-25) one would be motivated to determine the appropriate patient population by determining patients with the appropriate antibodies. Since Gaynor does not elaborate about which specific antibodies to test one would be motivated to use the teachings of Degiorgio. Thus one would be motivated to identify patients with anti-NR2 antibodies as

taught by Degiorgio (page 1190 2nd column, Figure 3) as recited in claim 46. One would be motivated to combine the teachings of the prior art to address the problem in the art – the treatment of lupus. Further, since Degiorgio teach that cerebrospinal fluid of patients with lupus was also tested (page 1190 2nd column last paragraph) one would be motivated to test for antibodies from the cerebrospinal fluid as recited in claim 47. Since Degiorgio noted that the antibodies may be produced in the brain or may cross the blood brain barrier (page 1191 paragraph connecting column 1 and 2) one would be motivated to also test for antibodies from blood as recited in claim 48. Since Gaynor teach a method for treating systemic lupus erythematosis in a subject in need of such treatment comprising administering to the subject at least one peptide which binds to an anti-double stranded DNA antibody (column 2 lines 20-25) and specifically teach the method for humans (column 6 lines 64-66) one would be motivated to administer peptides to humans with systemic lupus erythematosis as recited in claims 23,46. Since Gaynor specifically teach a peptide of sequence Asp-Trp-Glu-Tyr-Ser (claims 9,44, column 9 line 11) and use that specific peptide in Figure 3 and Degiorgio also recognize such peptide (abstract) one would be motivated to administer the peptide Asp-Trp-Glu-Tyr-Ser thus meeting the limitations recited in claims 51,55. Gaynor teach that the compositions can be administered using procedures known in the art including a variety of administration modes (column 7 lines 12-20). Gaynor further teach that the peptides can be delivered to the site of action by injection (column 7 lines 30-40). Degiorgio specifically teach that the NR2 receptors are present on neurons in the brain (page 1189 2nd column). Thus one would be motivated to administer the peptides to the brain as recited in claim 45. One would have a reasonable

expectation of success since Degiorgio recognize injections to the cortex (page 1190 first paragraph).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Although unclear (see 112 2nd) the mimetic referred to in claim 51 is interpreted as the peptide of claim 46.

***Response to Arguments - 103***

Applicants argue (page 7) that the references do not suggest using an agent comprising the amino acid sequence as claimed for inhibiting progression of cognitive dysfunction in a mammal diagnosed as exhibiting or as being at risk for lupus-induced cognitive dysfunction.

Applicant's arguments filed 4/12/10 have been fully considered but they are not persuasive.

Although Applicants argue (page 7) that the references do not suggest using an agent comprising amino acid sequence as claimed for inhibiting progression of cognitive dysfunction in a mammal diagnosed as exhibiting or as being at risk for lupus-induced cognitive dysfunction, it is unclear which specific feature is supposedly not taught by the prior art. In the instant case, Gaynor specifically teach a peptide of sequence Asp-Trp-Glu-Tyr-Ser (claims 9,44, column 9 line 11) and use that specific peptide in Figure 3 and Degiorgio also recognize such peptide (abstract) one would be motivated to administer the peptide Asp-Trp-Glu-Tyr-Ser. Thus the art clearly teaches the claimed agent and administration thereof. Gaynor expressly teach methods of

treating systemic lupus erythematosis ultilizing peptides (abstract). Since Gaynor teach a method for treating systemic lupus erythematosis in a subject in need of such treatment one would be motivated to treat such patients. Thus one would be motivated to patients with lupus. It is noted that such patients (patients with lupus) are at risk for lupus-induced cognitive dysfunction since as the name implies it is induced by lupus. Further, since Degiorgio teach that up to 80% of lupus patients experience symptoms including congnitive decline (page 1189 first paragraph) one would be motivated to treat those with lupus who have cognitive decline. Further, Degiorgio teach that in systemic lupus erythematosis (SLE) that antibodies against double-stranded DNA are a major contributor to disease (abstract) and correlate with disease (page 1189 first column). Thus as recited in applicants own claim 46 the detection of such antibodies identifies specific patient populations to treat.

***Prior art of Record***

The prior art previously made of record and not relied upon is considered pertinent to applicant's disclosure:

Gaynor et al (2005/0214852 as cited in IDS 2/19/09) – Gaynor teach detecting antibodies (claim 24,71).

Vojdani et al (US 2003/0100035) – Vojdani teach peptides comprising DWEYS (section 0040 example 8).

***Conclusion***

The 112 2nd rejection is a new rejection necessitated by applicants amendments. Claims were previously rejected under 103 based on the references cited herein. Since the claims have been amended and new claims added the rejection is updated. Thus applicants amendments have necessitated any new grounds of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654